

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (currently amended) A composition comprising a mature mocarhagin protein at least 95% free of other cobra proteins and comprising an N terminal amino acid sequence of ~~TNTPEQDXYLQAKKYZEFYVVVDNBM~~, wherein ~~X~~ is G or R, ~~Z~~ is L or I, and ~~B~~ is V, R or I chosen from:

- a) amino acids 192 to 221 of SEQ ID NO: 6;
- b) amino acids 192 to 221 of SEQ ID NO: 8;
- c) amino acids 192 to 221 of SEQ ID NO: 10;
- d) amino acids 192 to 221 of SEQ ID NO: 12;
- e) amino acids 192 to 221 of SEQ ID NO: 14.

2. (currently amended) The composition of claim 1, wherein said mocarhagin protein is full-length mocarhagin.

3. (currently amended) The composition of claim 1, wherein said mocarhagin protein is a fragment of ~~full-length~~ mature mocarhagin having mocarhagin proteolytic activity.

4. (currently amended) The composition of claim 1, wherein said mocarhagin protein exhibits an IC₅₀ of less than about 100 µg/mL in a neutrophil/HL60 binding inhibition assay.

5. (currently amended) The composition of claim 1, wherein said mocarhagin protein is characterized by at least one characteristic selected from the group consisting of:

- (a) a molecular weight of approximately 55 kDa under reducing conditions;
- (b) a molecular weight of approximately 55 kDa under nonreducing conditions;
- (c) an N-terminal amino acid sequence comprising
TNTPEQDRYLQAKKYIEFYVVVDNVMYRKY (SEQ ID NO: 1);
- (d) mocarhagin proteolytic activity;
- (e) the ability to inhibit platelet binding to vWF;
- (f) requirement of calcium ion for activity;
- (g) requirement of zinc ion for activity;
- (h) an activity substantially inhibited by excess EDTA; and
- (i) an activity substantially inhibited by high concentrations of DFP.

6. (currently amended) The composition of claim 1, wherein said mocarhagin protein is capable of cleaving a material selected from the group consisting of anionic polypeptides containing sulfated tyrosine residues, PSGL-I and GP Iba.

7. (original) A composition comprising a therapeutically effective amount of a composition of claim 1 and a pharmaceutically acceptable carrier.

8. (withdrawn) A method of treating an inflammatory disease comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

9. (withdrawn) A method of inhibiting selectin-mediated binding comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

10. (withdrawn) A method of isolating mocarhagin from venom, said method comprising:

- (a) subjecting a composition comprising cobra venom to a heparin affinity chromatography column;
- (b) subjecting the eluate from said heparin affinity column to a size exclusion column;

(c) subjecting the eluate from said size exclusion column to a Mono S column; and

(d) eluting said mocarhagin from said Mono S column.

11. (currently amended) A composition comprising a mature mocarhagin protein isolated from cobra venom by:

subjecting a composition comprising cobra venom to a heparin affinity chromatography column;

(b) subjecting the eluate from said heparin affinity column to a size exclusion column;

(c) subjecting the eluate from said size exclusion column to a Mono S column; and

(d) eluting said mocarhagin from said Mono S column; and wherein
and the mature mocarhagin protein comprises an N terminal amino acid sequence
chosen from:

a) amino acids 192 to 221 of SEQ ID NO: 6;

b) amino acids 192 to 221 of SEQ ID NO: 8;

c) amino acids 192 to 221 of SEQ ID NO: 10;

d) amino acids 192 to 221 of SEQ ID NO: 12;

e) amino acids 192 to 221 of SEQ ID NO: 14.

12. (original) The composition of claim 11 further comprising a pharmaceutically acceptable carrier.

13. (withdrawn) A method of treating an inflammatory disease comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

14. (withdrawn) A method of inhibiting selectin-mediated binding comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

15. (withdrawn) A composition comprising an antibody which specifically reacts with the mocarhagin of the composition of claim 1 or a fragment thereof having mocarhagin proteolytic activity.

16. (currently amended) The composition of claim 4₁ wherein said mocarhagin protein exhibits an IC₅₀ of less than about 1 µg/mL in a neutrophil/HL60 binding inhibition assay.

17. (currently amended) The composition of claim 1₁ wherein said mocarhagin protein is homogeneous.

18. (canceled)

19. (currently amended) The composition of claim 5₁ wherein said protein comprises the amino acid sequence of SEQ ID NO:6 from amino acid 192 to amino acid 621.

20. (original) A composition comprising a mocrhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:6;
- (b) the amino acid sequence of SEQ ID NO:6 from amino acid 24 to amino acid 621;
- (c) the amino acid sequence of SEQ ID NO:6 from amino acid 192 to amino acid 621;
- (d) fragments of the amino acid sequence of SEQ ID NO:6 encoding a protein having mocrhagin activity; and
- (e) the amino acid sequence encoded by the cDNA insert of clone NMM-1 deposited under accession number ATCC 209588; the protein being substantially free from other mammalian proteins.

21. (currently amended) The composition of claim 20₁ wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

22-26. (canceled)

27. (previously presented) A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

28. (original) The protein of claim 27 comprising a mature protein.

29. (original) A pharmaceutical composition comprising a protein of claim 20 and a pharmaceutically acceptable carrier.

30. (original) A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:8;

(b) the amino acid sequence of SEQ ID NO:8 from amino acid 24 to amino acid 439;

(c) the amino acid sequence of SEQ ID NO:8 from amino acid 192 to amino acid 439;

(d) fragments of the amino acid sequence of SEQ ID NO:8 encoding a protein having mocoarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-2 deposited under accession number ATCC 209589; the protein being substantially free from other mammalian proteins.

31. (currently amended) The composition of claim 30, wherein said protein comprises the amino acid sequence of SEQ ID NO: 8.

32-36. (canceled)

37. (previously presented) A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 7 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

38. (original) The protein of claim 37 comprising a mature protein.

39. (original) A pharmaceutical composition comprising a protein of claim 30 and a pharmaceutically acceptable carrier.

40. (Currently amended) A composition comprising a mocoarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO: 10;
- (b) the amino acid sequence of SEQ ID NO: 10 from amino acid 24 to amino acid 613;
- (c) the amino acid sequence of SEQ ID NO: 10 from amino acid 192 to amino acid 613;
- (d) fragments of the amino acid sequence of SEQ ID NO: 10 encoding a protein having mocoarhagin activity; and
- (e) the amino acid sequence encoded by the cDNA insert of clone NMM-9 deposited under accession number ATCC 209586; the protein being substantially free from other mammalian proteins.

41. (currently amended) The composition of claim 40, wherein said protein comprises the amino acid sequence of SEQ ID NO: 10.

42-46. (canceled)

47. (previously presented) A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 9 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

48. (original) The protein of claim 47 comprising a mature protein.

49. (original) A pharmaceutical composition comprising a protein of claim 40 and a pharmaceutically acceptable carrier.

50. (original) A composition comprising a mocrhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 12;

(b) the amino acid sequence of SEQ ID NO: 12 from amino acid 24 to amino acid 521;

(c) the amino acid sequence of SEQ ID NO: 12 from amino acid 192 to amino acid 521;

(d) fragments of the amino acid sequence of SEQ ID NO: 12 encoding a protein having mocrhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-12 deposited under accession number ATCC 209585; the protein being substantially free from other mammalian proteins.

51. (currently amended) The composition of claim 50, wherein said protein comprises the amino acid sequence of SEQ ID NO: 12.

52-56. (canceled)

57. (previously presented) A protein produced according to a process comprising:

- (a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 11 operably linked to an expression control sequence; and
- (b) purifying the protein from the culture.

58. (original) The protein of claim 57 comprising a mature protein.

59. (original) A pharmaceutical composition comprising a protein of claim 50 and a pharmaceutically acceptable carrier.

60. (currently amended) A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO: 14;

- (b) the amino acid sequence of SEQ ID NO: 14 from amino acid 24 to amino acid 592;
- (c) the amino acid sequence of SEQ ID NO: 14 from amino acid 192 to amino acid 592;
- (d) fragments of the amino acid sequence of SEQ ID NO: ~~12~~ 14 encoding a protein having mocoarhagin activity; and
- (e) the amino acid sequence encoded by the cDNA insert of clone NMM-13 deposited under accession number ATCC 209584; the protein being substantially free from other mammalian proteins.

61. (previously presented) The composition of claim 60 wherein said protein comprises the amino acid sequence of SEQ ID NO: ~~12~~ 14.

62-66. (canceled)

67. (previously presented) A protein produced according to a process comprising:

- (a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 13 operably linked to an expression control sequence; and
- (b) purifying the protein from the culture.

68. (original) The protein of claim 67 comprising a mature protein.

69. (original) A pharmaceutical composition comprising a protein of claim 60 and a pharmaceutically acceptable carrier.

70. (original) A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO: 16;
- (b) the amino acid sequence of SEQ ID NO: 16 from amino acid 62 to amino acid 462;
- (c) fragments of the amino acid sequence of SEQ ID NO: 16 encoding a protein having mocarhagin activity; and
- (d) the amino acid sequence encoded by the cDNA insert of clone NMM-3 deposited under accession number ATCC 209587; the protein being substantially free from other mammalian proteins.

71. (currently amended) The composition of claim 70₁ wherein said protein comprises the amino acid sequence of SEQ ID NO: 16.

72-76. (canceled)

77. (previously presented) A protein produced according to a process comprising:

- (a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 15 operably linked to an expression control sequence; and
- (b) purifying the protein from the culture.

78. (original) The protein of claim 77 comprising a mature protein.

79. (original) A pharmaceutical composition comprising a protein of claim 70 and a pharmaceutically acceptable carrier.

80. (original) A composition comprising a mocrhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO: 18;
- (b) the amino acid sequence of SEQ ID NO: 18 from amino acid 197 to amino acid 621;
- (c) fragments of the amino acid sequence of SEQ ID NO: 18 encoding a protein having mocrhagin activity; and
- (d) the amino acid sequence encoded by the cDNA insert of clone NMM-9ek deposited under accession number ATCC 209583; the protein being substantially free from other mammalian proteins.

81. (currently amended) The composition of claim 80, wherein said protein comprises the amino acid sequence of SEQ ID NO: 18.

82-86. (canceled)

87. (previously presented) A protein produced according to a process comprising:

- (a) in a suitable culture medium, growing a culture of a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 operably linked to an expression control sequence; and
- (b) purifying the protein from the culture.

88. (original) The protein of claim 87 comprising a mature protein.

89. (original) A pharmaceutical composition comprising a protein of claim 80 and a pharmaceutically acceptable carrier.

96. (withdrawn) A method of treating a condition characterized by P- or E-selectin-mediated intercellular adhesion comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

97. (withdrawn) A method of treating a condition characterized by P- or E-selectin mediated intercellular adhesion comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

98. (withdrawn) The method of claims 96 or 97 wherein said condition characterized by P- or E-selectin mediated intercellular adhesion is selected from the group consisting of: myocardial infarction, vessel restenosis, thrombosis, bacterial or viral infection, metastatic conditions, inflammatory disorders such as arthritis, acute respiratory distress syndrome, asthma, emphysema, delayed type hypersensitivity reaction, systemic lupus erythmatosus, thermal injury, autoimmune thyroiditis, experimental allergic encephalomyelitis, multiple sclerosis, diabetes, Reynaud's syndrome, neutrophilic dermatosis, inflammatory bowel disease, Grave's disease, glomerulonephritis, gingivitis, periodontitis, hemolytic uremic syndrome, ulcerative colitis, Crohn's decease, necrotizing enterocolitis, granulocyte transfusion associated syndrome, and cytokine-induced toxicity.

99. (withdrawn) A method of treating a condition characterized by P- or E-selectin mediated intercellular adhesion comprising administering a therapeutically effective amount of a composition of any one of claims 29, 39, 49, 59, 69, 79, or 89 to a mammalian subject.